学位申請論文

片山一道

主論文

Genetic Differentiation of Blood Polymorphic Systems among Three Isolated Human Populations in Central Japan.

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An isolate population, which more or less genetically deviates from neighboring populations, sometimes comprises subpopulations with different gene frequency distributions within it. It is not always easy to, however, assess the degree of genetic diversity among subpopulations. Choosing small isolated population, on which biological, demographic, historical, and marital data are relatively easy to accumulate, may have various advantages in solving this problem. There are already some reports on genetic differentiation among small isolated populations, for example, from Amerindian tribes (Neel & Ward, 1970), Italian alpine villages (Cavalli-Sforza, 1969), Bougainville islanders (Friedlaender, 1975), etc.. In Japan, however, relatively undisturbed populations whose mode of life reflects the circumstances under which the genetic diversity has been developed and whose population sizes are still kept considerably large are rapidly decreasing in number. With respect to the local genetic differentiation in Japan, the reports by Nei & Imaizumi (1966abc) are the only series of extensive studies so far made, although these deal with the ABO system alone.

During the past five years, we have been engaged in an intensive genetic study of the three villages in Mie Prefecture in central Japan. These are small isolated populations which seem to meet the above qualification.

This paper is an attempt to assess the degree of genetic differentiation by the coefficient of gene diversity (Nei, 1973) in the small area where the three populations exist and to specify the factors responsible for their differentiation.

A series of studies have already been made on blood polymorphism distribution in Kamishima Island (Toyomasu et al., 1977) and in Toshi-jima Island (Toyomasu & Katayama, 1979), on the demographic and breeding structure in Kamishima Island (Katayama et al., 1978), and on the genetic relations among the three populations (Katayama & Toyomasu, 1979). The information sources of this paper are mostly these.

POPULATIONS

1. Geographic, Demographic, and Genetic Features

Fig. 1 shows the location of the study populations. The villages of Kamishima, Toshi, and Momotori had respective populations of 1043, 2890, and 1571 at the time of survey (1975). They belong to Toba City of Mie Prefecture and are also adjacent to Aichi Prefecture. These villages have been inhabited since the Kofun period (about the 4-7th c.) and were occupied in 1889 respectively by 860, 2556, and 978 people (Nakaoka ed., 1970). The inhabitants live by fishery in Kamishima and Toshi, and by semi-fishery and

semi-agriculture in Momotori. Traditionally there have been few facilities of communication between them except via Toba, and at least during last 100 years only a few intervillage migrations have been recorded even between Toshi and Momotori located on the same island. However, taking into account the ethnographical study (Nakaoka ed., 1970), it is difficult to assume that these villages have been originated from genetically much different ancestral populations.

According to Katayama et al. (1978), the Kamishima population has been highly isolated geographically and reproductively for a long time, characterized by extremely high endogamy rate (91.6%) and mean inbreeding coefficient (0.0218-0.0578). Such situation is presumably the case also with the Toshi and Momotori populations.
Therefore, each village may be regarded as an isolate, unit population of breeding. Katayama & Toyomasu (1979) reported that, as expected from the geography, Toshi and Momotori appeared to be in somewhat closer relation in intervillage migration and genetic distance than with Kamishima, but not in a manner proportional to the geographic proximity among them, and concluded that the pattern of current genetic relation among these populations might be mostly due to the difference in intervillage migrations and to random factors and that the island model was applicable to the genetic

divergence in the study area. Toyomasu et al. (1977) and Toyomasu & Katayama (1979) reported that gene frequency distributions in some blood polymorphic systems for these populations were unique in comparison with those from Mie Prefecture, and that these genetic uniqueness might result from random genetic drift.

2. Genetic Data

Table 1 shows the population size and the sample size of each village. Thanks to the reliable sampling, the data may be regarded as representing the actual genetic compositions of the populations. The data on the ABO blood group, two serum proteins (Hp and Tf), and eight red cell enzymes (AcP, PGM_1, PGD, ADA, EsD, GPT, GOT, and PHI) are used in the analysis. The MN, Rh-Hr, Gm, and Km systems are excluded because of the lack of sufficient data or because of the significant deviation from the Hardy-Weinberg equilibrium. The LDH, PGK, AK, and PepA systems are also excluded, for no variant types are found in the study populations.

Table 2 gives the phenotype frequencies of these systems in the three populations. Of these systems, ABO, Hp, Tf, AcP, PGM_1, PGD, ADA, EsD, GPT, and GOT are polymorphic in all three populations, whereas PHI is slightly polymorphic only in the Kamishima population.

Table 3 shows the gene frequencies for the three

populations, their pooled population, and Mie and Aichi Prefectures, the variance of gene frequency among the three populations, and the ranges of frequencies of corresponding alleles in the general Japanese. The data of Mie and Aichi Prefectures and the Japanese ranges are adopted from the JIBP Synthesis II (Matsunaga chief ed., 1975).

Gene frequencies are calculated by Bernstein's method for ABO and by the gene counting method for the other systems. No modification from familial relationships such as sibling correlation is made since the sample sizes are large enough and Katayama et al. (1978) have already estimated the mean inbreeding coefficient.

RESULTS

1. Genetic Characteristics

Table 3 reveals: 1) In the three populations, the gene frequencies of Hp^1, $Tf^{var.}$, Gpt^2, PGD^c, EsD^2, ADA^2, and $Got^{var.}$ tend to deviate from the normal range so far reported from Japan. The variation of allele frequencies in the study area is remarkable. Similar results have been reported by many researchers dealing with isolates (Salzano et al., 1977; Friedlaender, 1975; etc.).

2) The allele frequencies in the Hp, PGM_1, and PGD systems in the pooled populations are especially closer to those in Mie Prefecture than those in Aichi Prefecture, while those in the ABO and ADA systems are in reverse.

2. Heterogeneity in Genotype (or Phenotype) Frequency Distributions

For each system, the genotype distributions among populations can be compared by means of the mXn contingency χ^2 analysis (Snedecor, 1956). This comparison tests the null hypothesis that the proportions of genotype frequencies are homogeneous among populations. If the expected value of any genotype class is less than 10, such a class is regrouped with others so that the new class will have an expected value greater than 10. Since this procedure is not possible in the GOT and PHI systems in which the genotypes in almost all persons are homozygote 1-1, no χ^2 values are computed for these systems.

Table 4 shows the results of this comparison. The χ^2 values are significant for all systems except the AcP system. Especially, the χ^2 values for the Hp, PGM_1, ADA, and GPT systems are significant also at the 0.1% level. Although the AcP system does not show a significant heterogeneity among the populations, it will be demonstrated

in the later section that its gene differentiation does not show a significant deviation from those of the other systems either.

These results suggest that the three populations are significantly different in the genotype (or phenotype) distributions of almost all the systems analyzed.

Furthermore, since each system analyzed here can be considered independent, the χ^2 values can be added together to give an overall comparison of the genotype distribution among the populations. The total χ^2 is much significant ($\chi^2 = 232.02$, $p<0.001$).

Do these differences correspond to those in the gene frequencies among the three populations?
Strictly speaking, a difference in genotype frequency may also result from variation in the mating practice, e.g. assortative mating, inbreeding, etc., and from sampling error. In the study area, however, the differences in genotype frequency may be expected to result exclusively from the differences in gene frequency among the populations, for the following reasons: 1) None of the systems in each population significantly deviates from the Hardy-Weinberg expectation so chosen. 2) Probably there has been little variation in the mating practice among the three populations. 3) The sample size for each system is fairly large.

3. Wahlund's Effect

When subpopulations have different gene frequencies, the overall increase in the proportion of homozygotes is called Wahlund's effect. Here it is examined whether there exists Wahlund's effect in the study area or not.

The local deviation from the Hardy-Weinberg equilibrium is estimated for a codominant locus by the formula:

$$F_i = 1 - \frac{H_i}{2p_iq_i},$$

where H_i is the observed proportion of heterozygotes at locus i, and p_i and q_i are the corresponding two allele frequencies.

A positive value of F_i indicates the excess of homozygote and a negative the excess of heterozygote.

Table 5 shows the F_i values of 10 codominant systems for the three populations and their pooled population. Although the three populations give negative values in 4 or 5 systems, their pooled population shows negative values only in 2 systems. Although all the populations show positive mean values of F_i, their pooled population's mean is the highest; the pooled population has heterozygosity less than expected. It is also interesting that the three populations show low but still positive mean F_i values, i.e. display weak excesses of homozygotes.

As suggested by Harpending et al. (1973), its cause may be

attributable to the demographic features that these populations have been highly endogamous.

Thus, the overall increase in the proportion of homozygotes demonstrates that Wahlund's effect exists in the study area.

4. Degree of Genetic Differentiation

There are two popular indices to formulate in a single figure the degree of genetic differentiation among sub-populations, viz. the fixation index (F_{ST}) by Wright (1951) and the coefficient of gene diversity (G_{ST}) by Nei (1973). These indices, in essence, measure the degree of Wahlund's effect caused by genetic differentiation among subpopulations.

As pointed out by Nei (1965), in the presence of more than 2 alleles at a locus, F_{ST} no longer holds valid except in special cases of random variation with no selection, whereas G_{ST} is also applicable to the comparison of the gene differentiation in a single locus, irrespective of the number of alleles and of the evolutionary forces.
Additionally, for a locus with only two alleles, G_{ST} becomes identical with F_{ST} (Nei, 1973) and, for a locus with multiple alleles, G_{ST} is practically equivalent to F_{ST} (Nei, 1977). Therefore, G_{ST} is more suitable for general use than F_{ST}.

Using the gene diversity of the total population (H_T), within subpopulations (H_S), and among subpopulations (D_{ST}),

G_{ST} is calculated as:

$$G_{ST} = D_{ST}/H_T,$$

$$D_{ST} = H_T - H_S,$$

$$H_T = 1 - \sum_{i=1}^{r} x_i^2$$

$$H_S = 1 - \sum_{k=1}^{s} \sum_{i=1}^{r} x_{ki}^2 / s,$$

where x_i is the mean gene frequency of the i-th allele, x_{ki} the gene frequency of the i-th allele in the k-th subpopulation, r the number of alleles in a locus, and s the number of subpopulations concerned.

When gene frequencies are completely identical among subpopulations, G_{ST} becomes zero; and when there are complete fixations in different subpopulations with different alleles, G_{ST} becomes 1.

From the gene frequencies for the pooled population ($\bar{p}$) and the variances of gene frequency among the three populations (σ) in Table 3, F_{ST} is calculated as:

$$F_{ST} = \frac{\sigma}{\bar{p}(1-\bar{p})}.$$

Following Lewontin & Krakauer (1973), for a locus with multiple alleles, instead of F_{ST} is used the value obtained by dividing the total F_{ST} of all alleles in the locus by r-1, where r is the number of alleles.

The parameters, H_T, H_S, D_{ST}, G_{ST}, and F_{ST}, for all systems analyzed are shown in Table 6.

As expected from the heterogeneity tests, the Hp and ADA systems show particularly higher values of G_{ST}, the PHI system a fairly high value, and the AcP system the lowest. The other seven systems show the G_{ST} values in the order of 10^{-3}, and are similar to one another.

The heterogeneity of gene differentiation by system is tested with the method by Lewontin & Krakauer (1973). This method was designed to compare the observed variance of F_{ST} with the expected variance caused by sampling error alone. Levontin & Krakauer (1973) gave the expected variance of F_{ST} as:

$$\sigma_F^2 = k \cdot \overline{F_{ST}}^2 / (n-1),$$

where k is approximately 2 for values of F_{ST} in the range 0-0.05, which includes the values in this study, $\overline{F_{ST}}$ is the mean value of F_{ST}, and n is the number of populations concerned.

Application of the above formula to the F_{ST} values in Table 6 gives the expected variance (σ_F^2) of 3.6845×10^{-5}, whereas the observed variance (s_F^2) is 1.9662×10^{-5}. The difference between them is not significant ($s_F^2/\sigma_F^2 = 0.5336$, $0.5 < p$) by the F-test. (If Robertson's (1975) revised method is applied, σ_F^2 becomes even greater and accordingly

the s^2_F/σ^2_F value becomes smaller.)
In other words, the seeming heterogeneity of the F_{ST} values by system is attributable only to sampling variance. Accordingly, it is reasonable to assume the homogeneity of F_{ST} for all the systems analyzed in the study area.

The result suggests that nonselective aspects of population structure such as random factors and migration is responsible for the present genetic differentiation.

Furthermore, the mean G_{ST} value of 0.00607 indicates that the absolute genetic difference among the study populations (Mean D_{ST}) is 0.6% of the total genetic variation (Mean H_T) in the study area. This value suggests that only a small fraction of the total genetic variation is attributable to the genetic difference among the populations.
Similar results have been also reported for the genetic differentiation among major races, tribes, or other populations in the world (Nei & Roychoudhury, 1974; Roychoudhury, 1975 and 1977; etc.).

5. Comparison of G_{ST} with Those from Other Levels of Human Population

For comparison, the G_{ST} values are calculated here from 7 or 9 systems for the following 3 hierarchic levels of Japanese, whose data are taken from JIBP Synthesis II

(Matsunaga chief ed., 1975):

1) The genetic differentiation in the Southwest Japan; among the four general populations from Sakishima (Ishigaki and Miyako Islands), Naha City, Amami-Oshima (mostly from Naze City), and Kagoshima City, among which the interpopulation migration may not have been so open due to the isolation by sea.

2) The genetic differentiation among 3 districts, Tohoku, Kinki, and Kyushu, of Japan.

3) The genetic differentiation among the Ainu, Kinki, and Sakishima populations.

Table 7abc give the parameters for these genetic differentiations. The results reveal that the study area displays the genetic differentiation much significantly greater than that among the 3 districts ($F = 8.60$, $p<0.01$), significantly greater than that in the Southwest Japan ($F = 6.96$, $p<0.05$), and, though not significantly ($F = 0.32$, $0.5<p$), a little smaller than that among the Ainu, Kinki, and Sakishima populations.

On the degree of genetic differentiation for various hierarchic levels from the world, there are already some reports; the G_{ST}-values are 0.14 among the three major races (Nei, 1975), 0.08 among some South Amerindian tribes (Rothhammer et al., 1976), and 0.006 among 7 local general populations from all over India (Roychoudhury, 1977).

Comparisons with these reports are however unwarranted, since the randomness of sampling of the systems analyzed is not certain.

Accordingly, the study area shows no genetic differentiation in a proportion to its hierarchic level, but such a situation may be observable also in the above Amerindian tribes and other populations (Workman & Niswander, 1970; Friedlaender, 1975; etc.).
In general, isolated populations show the tendency to a great genetic differentiation through random genetic drift and founder effect due to the high degree of isolation and their relatively amall population sizes.

6. Interpopulation Variation Patterns in Genotype Frequencies

For each system, the interpopulation variation pattern in genotype frequencies is detectable from heterogeneity tests between pair combinations of populations by means of the χ^2 analysis. The same modification procedure as in the previous section (Result 2) is followed, and the PHI system is not tested.

Table 8 presents the χ^2 values between pair combinations of the three villages and Mie, which is assumed to be the ancestoral population of the three villages from the historical evidence presented by Nakaoka ed. (1970).

This analysis leads to a classification of the systems by their interpopulation variation patterns in genotype frequencies as follows:

A. The non-variable types;

1) nearly homogeneous throughout the four populations ..... AcP,

2) homogeneous among the three island populations ..... GOT.

B. The type in which the frequency sequence corresponds to the geographic location of the populations, i.e. the genotype frequencies differ most greatly between Kamishima and Mie ..... GPT and ADA.

C. The type in which geographically the most distant populations, Kamishima and Mie, are most similar in the genotype frequencies ..... PGM_1.

D. The other types;

1) homogeneous both between Kamishima and Toshi and between Kamishima and Mie ..... ABO and EsD,

2) homogeneous both between Kamishima and Momotori and between Toshi and Mie ..... Hp,

3) homogeneous both between Kamishima and Toshi and between Momotori and Mie ..... PGD,

4) homogeneous among Kamishima, Momotori, and Mie, and Toshi alone has a fairly distant genotype frequency ..... Tf.

The result suggests that all systems tested are likely to vary in the most different ways possible, that is to say, the interpopulation variation patterns in the genotype frequencies are strikingly irregular.
This means that the genetic differentiation among the populations in the study area is apparently of random nature, just as indicated among the villages of Amerindian tribes such as Yanomama and Makiritare (Neel & Ward, 1970), Bougainville islanders (Friedlaender, 1975), and some Ge-speaking peoples (Salzano et al., 1977).

7. Genetic Variability

The genetic variability in a given population can be estimated by the proportion of polymorphic loci to all loci analyzed and by that of loci which one can expect to find as in heterozygous state in a given individual.
This study employs the latter, which, at the same time, indicates the degree of genetic fixation of a population.

The heterozygosity of a population at a particular locus (d) is $1 - \sum_{k=1}^{r} p_k^2$, where r is the number of alleles at that locus and p_k is the frequency of the k-th allele.
Then the heterozygosity of a population over n different loci (D) is computed as the mean over all loci, i.e.
$D = \frac{1}{n} \sum d_i$.

Table 9 presents the d values of seven systems and the D values for the three populations and their pooled population as well as those from Japanese populations of various sizes and at different hierarchic levels.
Since the randomness of sampling of the seven systems analyzed here is not certain, comparisons with other reports are unwarranted.

The study populations and their pooled population have the highest D values resembling one another, followed by the general populations of Tokyo and Mie Prefecture and by the Ainu and "Matagi" who lives in the mountains of north eastern Japan. These results suggest that the study populations have high genetic variabilities, or display low genetic fixation.

It is said that, in general, the higher the inbreeding and the smaller the population size is, the lower genetic variability a population will show, as the result of genetic fixation through random factors. In the present populations, the high genetic variabilities seem to disagree with the expectation inferred from the high inbreeding coefficient reported in Kamishima Island (Katayama et al., 1978).
However, as pointed out by Spiess (1977), populations which are strongly influenced by random factors may not necessarily decrease their genetic variabilities.
Even if the inflow of foreign genes is very limited, random variations may not always be accompanied by poor genetic

variability as long as most of the variations depend on random genetic drift rather than on founder effect.
Therefore, the result may be interpreted as a counter basis for regarding founder effect as a major factor in the present genetic diversity.

DISCUSSION

What factors are responsible for the genetic differentiation in the study area?
To specify the factors responsible for the present case, a synthetic view is taken here on the basis of what have been revealed in this study and in the previous studies.

In general, a genetic differentiation among isolated populations appears to be resulted by the following factors:
A) Factors producing genetic differentiation; 1) recurrent mutation, 2) selective forces acting at different intensities on different populations, and 3) such random factors as random genetic drift, founder effect, and bottle neck effect.
B) Factors retarding genetic differentiation; 1) selective force acting at a similar intensity on different populations and 2) migration.

In South Amerindian tribes, about a half of the genetic differentiation among villages was ascribed to founder effect

(Neel & Ward, 1970) and, in the Papago Indians, a large proportion of the genetic diversity among groups was attributed to intergroup migration and to inflow of foreign genes (Workman & Niswander, 1970). Furthermore, in Bougainville islanders, the genetic diversity among populations might be caused by mainly random genetic drift (Friedlaender, 1975). To the best of my knowledge, there is no report that any kind of selective force, recurrent mutation, and bottle neck effect have largely contributed to the genetic differentiation among human populations. It has also been said that, in the case of blood polymorphic systems, the variations in a large amount of systems may be maintained without any selective force in a population.

In relation to the above factors, the present study revealed: 1) The high genetic variabilities degrade the probability of founder effect as a major factor in the genetic differentiation. 2) The similarity in the degree of gene differentiation in all systems suggests that any kind of selective force is little responsible for the genetic differentiation. Further, Katayama et al. (1978) and Katayama & Toyomasu (1979) supply the bases for inferring the following: 3) Because of considerably small population sizes, frequent occurrence of mutations and their significance in the production of genetic variation may be assumed to be slight. 4) Since the study populations had kept their sizes

in a balanced state presumably for at least several hundred years prior to the rapid increase in the present century, it is difficult to assign any part of the genetic differentiation to bottle neck effect.

Hence, it is suggested that the genetic differentiation in the study area has mainly resulted from the remaining factors, random genetic drift and migration.
This agrees with the present result that the interpopulation variation patterns in genotype frequencies apparently show the random nature of the gene differentiation, and also with the conclusion of the previous report (Katayama & Toyomasu, 1979) that, although the migrations may have been relatively rare in the study populations, these are probably more or less responsible for the genetic diversity.

If only the random genetic drift functions to produce genetic differentiation without any migrations, the gene differentiation (G_{ST}) after t generations can be expected to be

$$G_{ST} = 1 - (1 - 1/2\overline{Ne})^{t},$$

where $\overline{Ne}$ is a harmonic mean of effective population size (Ne) over t generations (Wright, 1969).

Assuming that the study populations were settled in the Kofun period, some 1500 years ago, and that 1 generation time is 30 years at present (Katayama et al., 1978) and probably less before, t becomes at least about 50.

As Ne can be assumed to be about 30% of the population for isolates in Japan (Katayama, 1975), Ne may be taken roughly as 300, which is about 30% of the smallest population of the three villages at the beginning of the Meiji era.
Then, G_{ST} is expected to be at least 0.0669.
This value is by far larger than the mean G_{ST} value observed in the actual populations. This discrepancy may be mostly attributed to the retarded genetic differentiation, which is probably caused mostly by the intervillage migrations in this particular case.

The rate of migration (m) per generation can be estimated by Wright's formula (Wright, 1969);

$$m = 1 - \sqrt{2Ne \cdot F_{ST} / \{(2Ne - 1) \cdot F_{ST} + 1\}}.$$

If Ne and F_{ST} are taken as 300 and 0.006 respectively, then m is estimated at 0.1147. This value is fairly small as compared with other isolates in Japan (Katayama, 1975) and appears to be nearly equivalent to the miration rate, about 0.08, calculated from the endogamy rate in Kamishima Island (Katayama et al., 1978). Although the migration rate is relatively low in the present case, migrant individuals (Ne·m) become about 30 persons. Even if effective migration rate (me) is a little less than m, the coefficient of breeding isolation (Ne·me) seems to be by far greater than 4, which is the critical value; Wright (1969) suggested that the effect

of migration is not negligible in populations with an isolation index greater than this value. Weiss & Maruyama (1975) also suggested in their computer simulation that with greater migration, the genetic distances would be affected noticeably in even a short period. Therefore, in the study area, the migrations may have retarded the potential genetic differentiation due to random genetic drift at a considerable intensity.

Thus, it may be concluded that the genetic differentiation in the study area has been mainly resulted from random genetic drift and migration, that is, the greater part of the genetic diversity has been produced by random genetic drift and the potential differentiation has been retarded mostly by migration including some intervillage migrations.

SUMMARY

This paper attempts to assess the degree of genetic differentiation among three adjacent isolated populations from Mie Prefecture, Japan, to specify the factors mainly responsible for their differentiation, and to compare the result with those obtained at different hierarchic levels of human populations in Japan.

The assessment of the degree of genetic differentiation is made on the gene frequencies of 11 blood polymorphic systems and by means of the coefficient of gene diversity (Nei, 1973).

The following results are obtained:

1) The three populations are significantly different in the genetic composition.

2) Wahlund's effect is seen among the study populations.

3) The genetic differentiation among the study populations is found to be 0.6% of the total genetic variation.

4) The present island area displays the genetic differentiation by far greater than that among three districts, Tohoku, Kinki, and Kyushu, of Japan and somewhat smaller than that among the Ainu, Kinki, and Sakishima populations.

5) The interpopulation variation patterns in the genotype frequencies strikingly vary from one system to another.

6) No poverty of genetic variability is found in the study populations.

From the results of the present and previous studies (Katayama et al., 1978; Katayama & Toyomasu, 1979), the following conclusion can be drawn: The major part of the genetic differentiation among these populations has resulted from random genetic drift and migration including some inter-village migrations.

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REFERENCES

1) Cavalli-Sforza, L. L.: Genetic drift in an Italian population. Sci. Amer., 221: 30-37 (1969)

2) Friedlaender, J. S.: Patterns of Human Variation; The Demography, Genetics, and Phenetics of Bougainville Islanders. Harvard Univ. Press, Cambridge (1975)

3) Harpending, H., Workman, P., and Grove, J.: Local genotypic disequilibrium in a generalized island model. Hum. Biol., 45: 359-362 (1973)

4) Katayama, K.: Reproductive structure of Hatomajima population in Yaeyama Islands and its population genetic analysis. J. Anthrop. Soc. Nippon, 83: 309-319 (1975) (in Japanese with English summary)

5) Katayama, K., Toyomasu, T., and Matsumoto, H.: Genetic study on the local populations in Mie Prefecture. II. Population structure in Kamishima Island. J. Anthrop. Soc. Nippon, 86: 83-94 (1978) (in Japanese with English summary)

6) Katayama, K. and Toyomasu, T.: Genetic study on the local populations in Mie Prefecture. IV. The genetic relations among the Kamishima, Toshi, Momotori, and Toba populations. J. Anthrop. Soc. Nippon, 87: in press (1979)

7) Lewontin, R. C. and Krakauer, J.: Distribution of gene frequency as a test of the theory of the selective neutrality of polymorphisms. Genetics, 74: 175-195 (1973)

8) Matsumoto, H., Toyomasu, T., Sagisaka, K., Takahashi, K., and Steinberg, A. G.: Studies of red blood cell and serum polymorphisms among the Matagi. Jap. J. Hum. Genet., 22: 271-280 (1977)

9) Matsunaga, E. (ed. in chief): Distribution of polymorphic traits in Japanese and neighboring populations. Anthropological and Genetic Study on the Japanese, JIBP Synthesis, vol. 2: 71-204, S. Watanabe, S. Kondo, and E. Matsunaga eds.. Univ. of Tokyo Press, Tokyo (1975)

10) Nakaoka, S. (ed.): Toba Shima Shinshi. Toba City (1970) (in Japanese)

11) Neel, J. V. and Ward, R. H.: Village and tribal genetic distances among American Indians, and the possible implications for human evolution. Proc. Nat. Acad. Sci. USA, 65: 323-330 (1970)

12) Nei, M.: Variation and covariation of gene frequencies in subdivided populations. Evolution, 19: 256-258 (1965)

13) Nei, M.: Analysis of gene diversity in subdivided populations. Proc. Nat. Acad. Sci. USA, 70: 3321-3323 (1973)

14) Nei, M.: Molecular Population Genetics and Evolution. North-Holland, Amsterdam and New York (1975)

15) Nei, M.: F-statistics and analysis of gene diversity in subdivided populations. Ann. Hum. Genet., 41: 225-233 (1977)

16) Nei, M. and Imaizumi, Y.: Genetic structure of human

populations. I. Local differentiation of blood group gene frequencies in Japan. Heredity, 21: 9-35 (1966a)

17) Nei, M. and Imaizumi, Y.: Genetic structure of human populations. II. Differentiation of blood group gene frequencies among isolated populations. Heredity, 21: 183-190 (1966b)

18) Nei, M. and Imaizumi, Y.: Genetic structure of human populations. III. Differentiation of ABO blood group gene frequencies in small areas of Japan. Heredity, 21: 461-472 (1966c)

19) Nei, M. and Roychoudhury, A. K.: Genetic variation within and between the three major races of man, Caucasoids, Negroids, and Mongoloids. Am. J. Hum. Genet., 26: 421-443 (1974)

20) Robertson, A.: Gene frequency distributions as a test of selective neutrality. Genetics, 81: 775-785 (1975)

21) Rothhammer, F., Chakraborty, R., and Llop, E.: A collation of marker gene and dermatoglyphic diversity at various levels of population differentiation. Am. J. Phys. Anthrop., 46: 51-60 (1976)

22) Roychoudhury, A. K.: Genetic distance and gene diversity among linguistically different tribes of Mexican Indians. Am. J. Phys. Anthrop., 42: 449-454 (1975)

23) Roychoudhury, A. K.: Gene diversity in Indian populations. Hum. Genet., 40: 99-106 (1977)

24) Salzano, F. M., Neel, J. V., Gershowitz, H., and Migliazza, E. C. Intra and intertribal genetic variation within a linguistic group: the Ge-speaking Indians of Brazil. Am. J. Phys. Anthrop., 47: 337-348 (1977)

25) Snedecor, G.: Statistical Methods. Fifth edition. Iowa State Univ. Press, Ames (1956)

26) Spiess, E. B.: Genes in Populations. John Wiley & Sons, New York (1977)

27) Toyomasu, T., Katayama, K., Miyazaki, T., and Matsumoto, H.: Genetic study on the local populations in Mie Prefecture. I. Blood component polymorphisms in Kamishima Island. J. Anthrop. Soc. Nippon, 85: 311-323 (1977)

28) Toyomasu, T. and Katayama, K.: Genetic study on the local populations in Mie Prefecture. III. Blood component polymorphisms in Toshi-jima Island. J. Anthrop. Soc. Nippon, 87: in press (1979)

29) Weiss, K. M. and Maruyama, T.: Archeology, population genetics and studies of human racial ancestory. Am. J. Phys. Anthrop., 44: 31-50 (1975)

30) Workman, P.L. and Niswander, J. D.: Population studies on Southwestern Indian Tribes. II. Local genetic differentiation in the Papago. Am. J. Hum. Genet., 22: 24-49 (1970)

31) Wright, S.: The genetical structure of populations. Ann. Eugen., 15: 323-354 (1951)

32) Wright, S.: Evolution and Genetics of Populations; The Theory of Gene Frequencies, Vol. 2. Univ. of Chicago Press, Chicago (1969)

33) Yamamoto, M., Wada, T., Watanabe, T., Kanazawa, H., Saito, R., Kondo, M., Hosokawa, K., Masuda, M., Nakai, T., and Fujiki, N.: Genetic polymorphisms in four isolated communities in Kinki district. Jap. J. Hum. Genet., 17: 273-285 (1972)

Table 1

Total population and sample size of each village.

Population	No. of Inhabitants	Sample Size(%)
Kamishima	1043	617 (59.2)
Toshi	2890	890 (30.8)
Momotori	1571	572 (36.4)

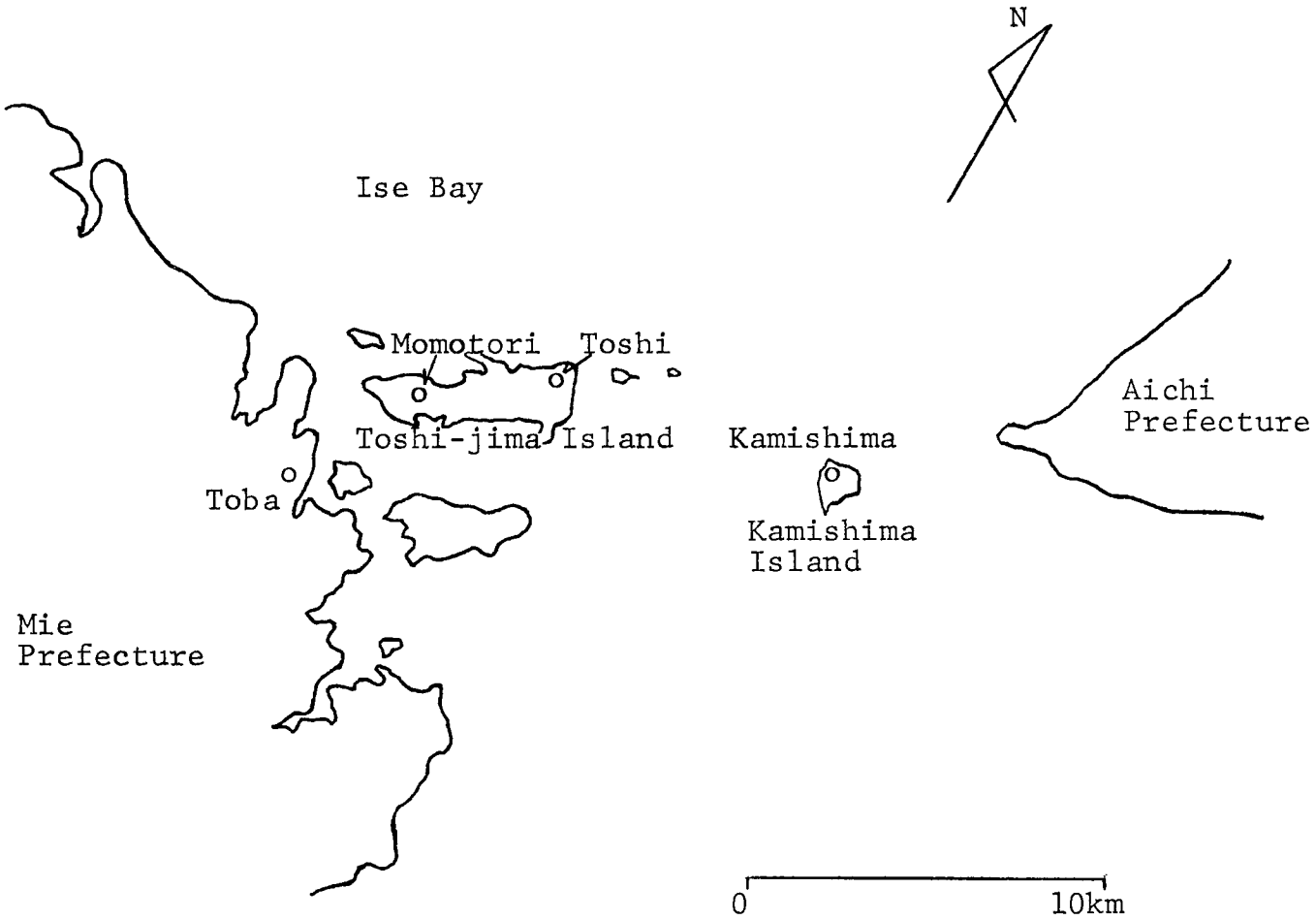

Fig. 1 Location of the Kamishima, Toshi, Momotori, and Toba populations.

Table 2

Phenotype frequencies of blood group, serum protein, and red cell enzyme systems.

System		Kamishima No.	Kamishima %	Toshi No.	Toshi %	Momotori No.	Momotori %
Blood Group							
ABO	A	157	38.1	381	44.1	230	41.2
	B	83	20.1	146	16.9	101	18.1
	AB	33	8.0	67	7.8	72	12.9
	O	139	33.7	270	31.3	155	27.8
	Total	412		864		558	
Serum Protein							
Hp	1-1	17	2.9	74	8.6	28	5.1
	2-1	184	31.7	347	40.5	157	28.4
	2-2	368	63.4	418	48.8	360	65.1
	0*	11	1.9	18	2.1	8	1.4
	Total	580		857		553	
Tf	C	555	95.7	846	98.7	533	96.4
	CD	10	1.7	8	0.9	20	3.6
	BC	13	2.0	3	0.4	0	0.0
	BB	2	0.6	0	0.0	0	0.0
	Total	580		857		553	
Red Cell Enzyme							
AcP	A	31	5.0	33	3.8	20	3.6
	BA	210	34.0	267	30.9	181	32.5
	B	376	60.9	564	65.3	356	63.9
	Total	617		864		557	

PGM_1	1-1	357	57.9	512	59.3	274	49.2
	2-1	206	33.4	283	32.8	221	39.7
	2-2	46	7.5	31	3.6	49	8.8
	7-1	5	0.8	26	3.0	12	2.2
	7-2	3	0.5	8	0.9	1	0.2
	6-1,6-2	0	0.0	4	0.4	0	0.0
Total		617		864		557	
PGD	A	337	74.6	636	73.6	450	80.8
	AC	108	23.9	212	24.5	98	17.6
	C	7	1.5	16	1.9	9	1.6
Total		452		864		557	
ADA	1-1	601	97.4	751	86.9	482	86.5
	2-1	16	2.6	108	12.5	73	13.1
	2-2	0	0.0	5	0.6	2	0.4
Total		617		864		557	
EsD	1-1	216	47.8	439	50.8	314	56.4
	2-1	191	42.2	348	40.3	210	37.7
	2-2	45	10.0	77	8.9	33	5.9
Total		452		864		557	
GPT	1-1	178	28.8	141	35.1	184	33.0
	2-1	291	47.2	206	51.2	288	51.7
	2-2	148	24.0	55	13.7	85	15.3
Total		617		402		557	
GOT	1-1	610	98.9	856	99.1	556	99.8
	2-1	7	1.1	6	0.7	1	0.2
	3-1	0	0.0	2	0.2	0	0.0
Total		617		864		557	

PHI	1-1	609	98.7	863	99.9	557	100.0
	2-1	8	1.3	0	0.0	0	0.0
	3-1	0	0.0	1	0.1	0	0.0
	Total	617		864		557	

*; Excluded from calculating the gene frequencies.

Note; See Toyomasu et al. (1977), for the detailed typing method of each system.

Table 3 Gene frequencies in the Kamishima, Toshi, Momotori, their pooled, and neighboring populations.

Allele		Gene Frequency KAM	TOS	MOM	Pooled	q^2	MIE	AICHI	Japanese No.*	Range
ABO	A	0.266	0.306	0.320	0.301	0.00039	0.266	0.270	64	0.167-0.431
	B	0.153	0.132	0.168	0.148	0.00024	0.186	0.175		0.119-0.213
	O	0.581	0.562	0.513	0.552	0.00072	0.548	0.555		0.395-0.627
Hp	Hp^1	0.192	0.295	0.195	0.237	0.00253	0.267	0.293	25	0.220-0.298
	Hp^2	0.808	0.705	0.805	0.763		0.733	0.707		0.702-0.780
Tf	Tf^C	0.977	0.994	0.982	0.985	0.00005	0.983		14	0.983-0.996
	Tf^D	0.008	0.005	0.018	0.010	0.00003	0.011			0.002-0.015
	Tf^B	0.015	0.002	0.0	0.005	0.00003	0.006			0.0 -0.006
AcP	p^A	0.220	0.193	0.198	0.203	0.00014	0.205	0.201	19	0.174-0.270
	p^B	0.780	0.807	0.802	0.797		0.794	0.799		0.729-0.826
PGM_1	PGM_1^1	0.750	0.773	0.701	0.746	0.00087	0.780	0.791	20	0.698-0.809
	PGM_1^2	0.244	0.205	0.287	0.239	0.00114	0.217	0.205		0.188-0.300
	others	0.007	0.022	0.012	0.015	0.00005	0.003	0.004		0.0 -0.019
PGD	PGD^A	0.865	0.859	0.896	0.871	0.00026	0.915	0.921	15	0.890-0.951

ADA	ADA[1]	0.989	0.932	0.931	0.949	0.00070	0.972	0.968	14	0.968-0.990
	ADA[2]	0.011	0.068	0.069	0.051		0.028	0.032		0.010-0.032
EsD	EsD[1]	0.689	0.710	0.752	0.717	0.00058	0.650		4	0.636-0.668
	EsD[2]	0.311	0.290	0.248	0.283		0.350			0.332-0.364
GPT	Gpt[1]	0.524	0.607	0.589	0.568	0.00129	0.623		8	0.535-0.623
	Gpt[2]	0.476	0.393	0.411	0.432		0.376			0.376-0.465
GOT	Got[1]	0.994	0.995	0.999	0.996	0.0	0.989		8	0.985-0.994
	others	0.006	0.005	0.001	0.004		0.011			0.006-0.015
PHI	PHI[1]	0.994	0.999	1.0	0.998	0.0	0.995	0.996	13	0.989-0.997
	others	0.006	0.001	0.0	0.002		0.005	0.004		0.003-0.011

KAM; Kamishima, TOS; Toshi, MOM; Momotori.

*; The number of populations used for determining the range of allele frequency. The criteria for inclusion are; showing non-significant deviation from the Hardy-Weinberg equilibrium; having minimum sample size of 200; and being sampled from general populations.

Table 4

Chi-square values for the heterogeneity test of genotype (or phenotype) frequencies among the 3 populations.

System	χ^2	d.f.
ABO	17.63**	6
Hp	56.50***	4
Tf(2 classes)	13.40**	2
AcP	3.98	4
PGM_1(4 classes)	41.79***	6
PGD	10.63*	4
ADA(2 classes)	54.10***	2
EsD	10.83*	4
GPT	23.16***	4
Total	232.02***	36

*, significant at the level of 5%,

**, significant at the level of 1%,

***, significant at the level of 0.1%.

Table 5

Values of F_i deriving from heterozygote proportions in 10 codominant systems.

System	Kamishima	Toshi	Momotori	Pooled
Hp	-0.0439	0.0048	0.0814	0.0268
Tf	0.1022	-0.0236	-0.0141	0.0875
AcP	0.0105	0.0068	-0.0217	0.0019
PGM_1	0.0835	-0.0308	0.0113	0.0228
PGD	-0.0231	-0.0103	0.0563	0.0067
ADA	-0.0927	0.0181	-0.0179	0.0011
EsD	0.0154	0.0214	-0.0107	0.0145
GPT	0.0537	-0.0732	-0.0677	-0.0148
GOT	0.0756	0.0955	0.0	0.0125
PHI	-0.0924	0.0667	0.0	-0.0100
Mean	0.0099	0.0075	0.0017	0.0149

Table 6

Coefficient of gene differentiation among the 3 populations.

System	H_T	H_S	D_{ST}	G_{ST}	F_{ST}
ABO	0.58347	0.58169	0.00178	0.00305	0.00333
Hp	0.36177	0.35669	0.00508	0.01404	0.01399
Tf	0.02887	0.02870	0.00017	0.00589	0.00621
AcP	0.32311	0.32287	0.00024	0.00074	0.00086
PGM_1	0.38561	0.38354	0.00207	0.00537	0.00711
PGD	0.22427	0.22371	0.00056	0.00250	0.00231
ADA	0.09716	0.09570	0.00146	0.01503	0.01446
EsD	0.40556	0.40440	0.00116	0.00286	0.00286
GPT	0.4970	0.48811	0.00259	0.00528	0.00526
GOT	0.00777	0.00775	0.00002	0.00257	0.00251
PHI	0.00476	0.00471	0.00005	0.00946	0.00920
Mean	0.29131	0.28979	0.00152	0.00607	0.00619

Table 7a

Coefficient of gene differentiation among the populations of Sakishima, Naha City, Amami-Oshima, and Kagoshima City.

System	H_T	H_S	D_{ST}	G_{ST}
ABO	0.59249	0.59192	0.00057	0.00096
Hp	0.39512	0.39318	0.00194	0.00491
Tf	0.01094	0.01091	0.00003	0.00274
AcP	0.36350	0.36319	0.00031	0.00085
PGM_1	0.40351	0.40270	0.00081	0.00201
PGD	0.13420	0.13405	0.00015	0.00112
ADA	0.03390	0.03385	0.00005	0.00147
GPT	0.49171	0.49118	0.00053	0.00108
GOT	0.02630	0.02630	0.0	0.00011
Mean	0.27241	0.27192	0.00049	0.00179

Table 7b

Coefficient of gene differentiation for 3 districts, Tohoku, Kinki, and Kyushu, in Japan.

System	H_T	H_S	D_{ST}	G_{ST}
ABO	0.58445	0.58405	0.00040	0.00068
Hp	0.38125	0.38089	0.00036	0.00094
Tf	0.01455	0.01455	0.0	0.0
AcP	0.33411	0.33409	0.00002	0.00006
PGM_1	0.34829	0.34768	0.00062	0.00177
PGD	0.16761	0.16748	0.00013	0.00076
ADA	0.04622	0.04619	0.00003	0.00055
Mean	0.26807	0.26785	0.00022	0.00083

Table 7c

Coefficient of gene differentiation among the Ainu, Kinki, and Sakishima populations.

System	H_T	H_S	D_{ST}	G_{ST}
ABO	0.58009	0.57948	0.00061	0.00105
Hp	0.37699	0.36825	0.00875	0.02320
Tf	0.01646	0.01643	0.00003	0.00188
AcP	0.38101	0.37710	0.00391	0.01027
PGM_1	0.35651	0.35337	0.00285	0.00798
PGD	0.13429	0.13316	0.00113	0.00841
ADA	0.04685	0.04678	0.00006	0.00137
Mean	0.27032	0.26780	0.00248	0.00774

Table 8

Chi-square values for the heterogeneity test of phenotype frequencies between pair combinations of the populations.

A. ABO and Tf systems

	KAM	TOS	MOM	MIE
KAM		4.58	9.10*	5.57
TOS	13.06***		11.56**	31.21***
MOM	0.37	8.40**		15.65***
MIE	0.55	8.12**	0.02	

Upper triangle; ABO blood group, d.f.=3.

Lower triangle; Tf serum protein, d.f.=1.

B. Hp and AcP systems

	KAM	TOS	MOM	MIE
KAM		38.63***	4.41	18.32***
TOS	3.35		35.89***	1.64
MOM	2.01	0.42		18.34***
MIE	1.98	1.73	2.04	

Upper triangle; Hp serum protein, d.f.=2.

Lower triangle; AcP red cell enzyme, d.f.=2.

C. GPT and PGM_1 systems

	KAM	TOS	MOM	MIE
KAM		15.11***	14.18***	30.59***
TOS	21.70***		0.70	5.59
MOM	9.64*	31.03***		9.28**
MIE	5.66	31.39***	29.78***	

Upper triangle; GPT red cell enzyme, d.f.=2.

Lower triangle; PGM_1 red cell enzyme, d.f.=3.

D. EsD and PGD systems

	KAM	TOS	MOM	MIE
KAM		1.18	9.99**	4.33
TOS	0.24		6.43*	14.49***
MOM	6.10*	9.86**		33.08***
MIE	17.35***	29.54***	4.82	

Upper triangle; EsD red cell enzyme, d.f.=2.

Lower triangle; PGD red cell enzyme, d.f.=2.

E. ADA and GOT systems

	KAM	TOS	MOM	MIE
KAM		49.67***	48.31***	6.97**
TOS	0.16		0.04	24.24***
MOM	3.76	3.00		23.35***
MIE	5.03*	8.90**	13.08***	

Upper triangle; ADA red cell enzyme, d.f.=1.

Lower triangle; GOT red cell enzyme, d.f.=1.

KAM; Kamishima, TOS; Toshi, MOM; Momotori.

*, $p<0.05$. **, $p<0.01$, ***, $p<0.001$.

Table 9 Comparison of genetic variability by heterozygosity (D).

System	Kamishima	Toshi.	Momotori	Pooled	Arihara[1)]	"Matagi"[2)]	Ainu[3)]	Mie Pref.[3)]	Tokyo[3)]
ABO	0.5679	0.5720	0.6069	0.5828	0.6251	0.5610	0.5660	0.5940	0.5853
Hp	0.3098	0.4160	0.3144	0.3617	0.2066	0.2864	0.2715	0.3914	0.4126
Tf	0.0458	0.0127	0.0355	0.0297	0.0119	0.0178	0.0334	0.0336	0.0080
AcP	0.3436	0.3111	0.3181	0.3236	0.3421	0.3178	0.4352	0.3260	0.3509
PGM_1	0.3786	0.3599	0.4258	0.3861	0.2465	0.2704	0.2926	0.3445	0.3497
PGD	0.2336	0.2425	0.1865	0.0047	0.0	0.1261	0.0824	0.1556	0.1421
ADA	0.0218	0.1273	0.1287	0.0968	-	0.0178	0.0544	0.0272	0.0964
Mean	0.2716	0.2916	0.2880	0.2859	0.2387*	0.2282	0.2479	0.2675	0.2779

*, The Arihara population may give the lowest value if the data for ADA are available.

1). Yamamoto et al. (1972),

2). Matsumoto et al. (1978),

3). Matsunaga chief ed. (1975).